Case Report

Hyperosmolar Hyperglycemic State in a Patient Receiving Corticosteroids in Palliative Care: A Case Report

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Abstract

Corticosteroids are commonly used in palliative care to relieve symptoms but have been associated with adverse effects such as hyperglycemia. Here, we report a patient with end-stage cancer who developed a hyperosmolar hyperglycemic state during administration of corticosteroids. Insulin therapy and fluid replacement ameliorated his symptoms. The course of this patient suggests that a hyperosmolar hyperglycemic state should be considered as a differential diagnosis when a patient with a history of diabetes mellitus showed lethargy during a course of corticosteroids.
(Keywords: corticosteroids, hyperosmolar hyperglycemic state, diabetes mellitus, palliative care)

Abbreviations used: CT: computed tomography, HHS: hyperosmolar hyperglycemic state

Introduction:

Corticosteroids are commonly administered in palliative care[1], and may cause glucose intolerance as an adverse effect, which can range from a new onset of diabetes mellitus to a hyperglycemic crisis[2, 3]. One form of hyperglycemic crises is a hyperosmolar hyperglycemic state (HHS), which is defined by severe hyperglycemia, high serum osmolality, and dehydration[4]. HHS is recognized as a major adverse effect of corticosteroids and generally requires urgent treatment. Here, we report a patient with end-stage cancer who presented with HHS during corticosteroid treatments for lethargy in a palliative care setting.

Case:

The patient was a 75-year-old man with type 2 diabetes mellitus. For his glucose control, he was on metformin, glimepiride, vildagliptin, and empagliflozin and had an HbA1c level of approximately 7%. One year and four months before admission, he was diagnosed with hilar cholangiocarcinoma (stage Ⅲ B, T2aN1M0). He underwent portal vein embolization followed by extended right hepatectomy with bile duct reconstruction. He received an adjuvant chemotherapy with tegafur, gimerasil, and potassium oteracil. Subsequently pulmonary and lymph node metastases developed. He received another regimen of chemotherapy with gemcitabine plus cisplatin. The treatment, however, was discontinued after a computed tomography (CT) scan two months before admission

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revealed progressive disease. The patient was, then, referred to our palliative care service.

The patient complained of lethargy and pain throughout his body. Hydromorphone (4 mg/day) and dexamethasone (2 mg/day) were orally administered for pain and lethargy, respectively. After commencing a course of opioids, he experienced nausea. It was considered likely that the nausea was due to adverse effects of hydromorphone, so the hydromorphone was switched to 50 mg/day of tapentadol orally. He complained of severe lethargy, and the dexamethasone was increased from 2 to 4 mg/day. With no improvement in symptoms, he was admitted to the palliative care unit.

The patient's poor prognosis with end-stage cancer was explained, and accepted by both the patient and his family. He expressed his desire to find a relief from the lethargy, return home, and live out his remaining time with dignity. The patient's systemic conditions were assessed, resulting in a score of 5 on the Palliative Prognostic Index (PPI)[5] and a score of 11.5 on the Palliative Prognosis Score (PaP Score)[6]. The former score PPI of 5 suggested that 6-week survival was predicted with a positive predictive value of 76%. The latter score PaP Score of 11.5 suggested that median survival of 11 days (95% CI = 7-14 days). In view of these findings, his prognosis was estimated to be at around three weeks.

On physical examination, his body temperature was 36.5℃, blood pressure 140/75 mmHg, pulse rate 90 per minute, and respiratory rate 24 per minute. Percutaneous arterial oxygen saturation was 96% on room air. Laboratory data on admission (Table 1) revealed severe hyperglycemia, dehydration, and electrolyte imbalance, while urinary ketone bodies were not detected. The serum osmolality was estimated to be as high as 348 mOsm. There was a moderate increase in the anion gap (15.1 mEq/L) and an increase in the corrected serum bicarbonate concentration (31 mmol/L). Based on these findings, the patient displayed both metabolic acidosis and metabolic alkalosis. The former indicated the presence of lactic acidosis associated with dehydration-induced central and peripheral circulatory impairment, but the lactic acid level was not measured. The latter was considered to be due to dehydration and vomiting. Because the increase in the anion gap was modest, the patient was diagnosed with HHS on the basis of hyperglycemia and high serum osmolality without ketone bodies. Chest and abdominal CT revealed lung and peritoneal metastases, and hydronephrosis of the right kidney (Figure 1).

Basic HHS treatment was commenced, consisting of intravenous insulin therapy and moderate-volume fluid replacement with normal saline (Figure 2). The treatment improved the hyperglycemia, lethargy, and nausea. The blood glucose levels were stabilized at 200-300 mg/dL and intravenous insulin was switched to subcutaneous insulin injection. On the 5th hospital day, serum osmolality showed a normal level of 278 mOsm. Subcutaneous insulin injection and fluid replacement were discontinued, and insulin was then switched to the subcutaneous administration of dulaglutide and nateglinide (Figure 2). Nausea and lethargy subsided, and he was discharged home on the 12th hospital day. Cachexia progressed, but he had no further complaints of lethargy and nausea. He died at home 16 days after discharge.

Table 1: Laboratory tests on admission

Urinalysis	Sugar	4+
	Protein	−
	Occult blood	±
	Ketone bodies	−
	Bilirubin	−
Hematologic test	White blood cells(/μL)	19570
	Neutrophils(%)	94.3
	Lymphocytes(%)	2.7
	Red blood cells(/μL)	4.54x106
	Hemoglobin(g/dL)	13.3
	Platelets(/μL)	240000
Biochemical test	Total protein (g/dL)	6.3
	Albumin(g/dL)	3.0
	Total bilirubin(mg/dL)	0.5
	AST(IU/L)	25
	ALT(IU/L)	13
	LDH(IU/L)	215
	Urea nitrogen(mg/dL)	77.9
	Creatinine(mg/dL)	1.71
	Sodium(mEq/L)	128
	Potassium(mEq/L)	5.7
	Chloride(mEq/L)	85
	CRP(mg/dL)	4.78
	Casual blood glucose	1162
	HbA1c(%)	12.5
Arterial blood gas	pH	7.411
	pCO2(mmHg)	44.7
	pO2(mmHg)	65.0
	HCO3-(mmol/L)	27.9

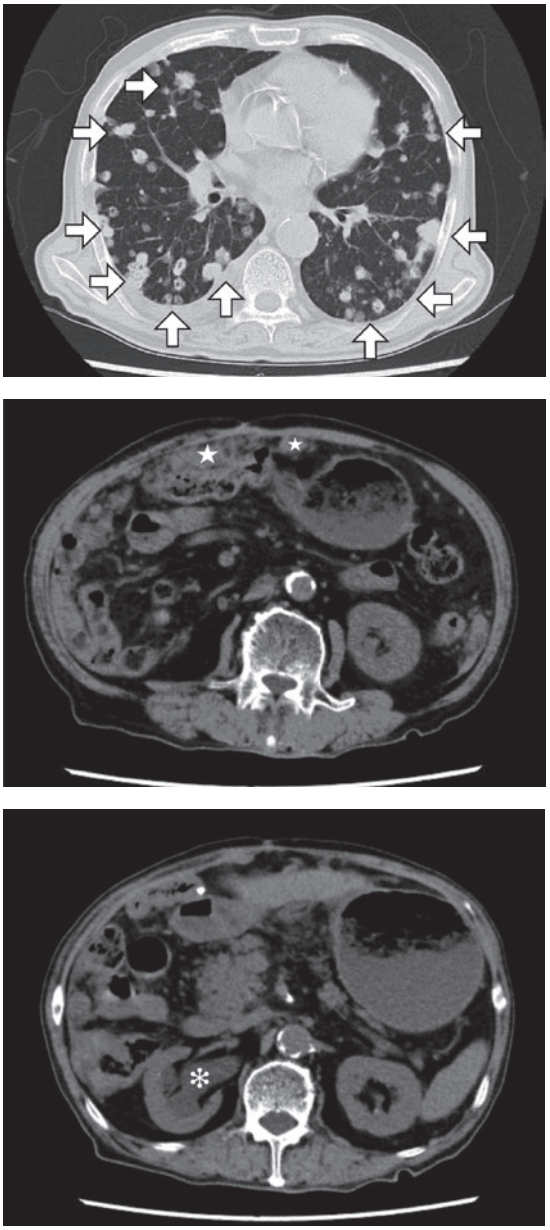

Figure 1: Computed tomography scans of chest and abdomen without contrast media, which indicate metastases to the lungs (arrows) and peritoneum (star), as well as right hydronephrosis (asterisk).

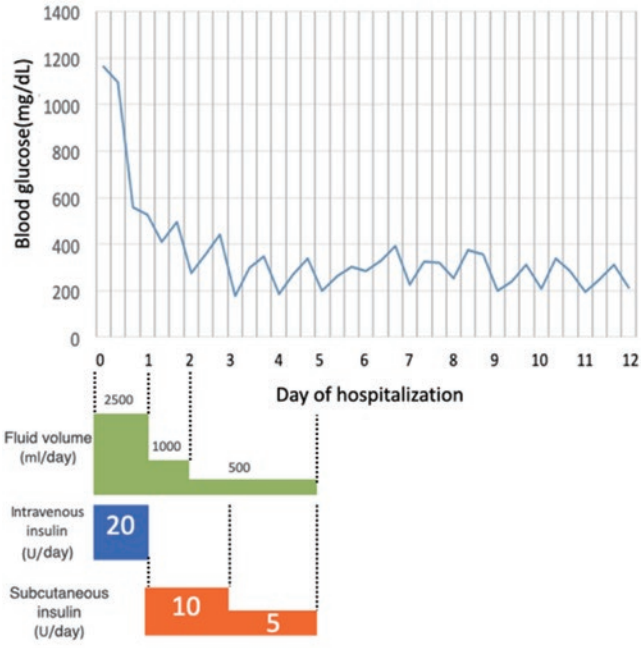

Figure 2: Blood glucose level, fluid replacement volume, and dose of intravenous or subcutaneous insulin administration during hospitalization.

Discussion:

This case suggests two clinical issues. First, we should be aware that HHS, as well as the onset or deterioration of diabetes, can be adverse effects of corticosteroids. Second, treating HHS can ameliorate HHS-associated symptoms (severe lethargy and nausea) and help the patient live out the remainder of his/her life with dignity. When patients receive corticosteroids in palliative care settings, vigilance for hyperglycemic crisis is important.

In anti-cancer chemotherapy, corticosteroid-induced hyperglycemia is frequently observed[7]. Administration of corticosteroids in palliative care can also lead to hyperglycemia[2, 3]. However, there is a paucity of literature regarding HHS in palliative care. It is unclear whether this is due to publication bias or HHS is truly rare in palliative care. When prescribing corticosteroids to patients with end-stage cancer, hyperglycemia and HHS should be considered as possible adverse effects. This patient had an increased risk of HHS because of history of diabetes mellitus. The number of diabetic patients has increased in palliative care[8]. The minimum dose of corticosteroids must be used to relieve symptoms[8, 9].

In non-palliative care contexts, HHS should be treated urgently. This patient and his family members desired relief from the patient's severe lethargy and nausea. HHS treatment rapidly ameliorated these complaints. However, it remains uncertain whether HHS in palliative care patients should always be treated as described in this case. Decisions should be made in a case-by-case manner, taking into account the patients' conditions and hope for their remaining time.

Fluid replacement warrants careful consideration. The fluid replacement protocol for HHS recommended by French et al.[4] is well-acknowledged, in which relatively large-volume fluid replacement is recommended. However, large-volume fluid replacement in terminally ill patients can exacerbate physical symptoms such as peripheral edema. It also increases sputum, being bothersome for patients[10]. Thus, depending on the patients' conditions, treating HHS poses the risk of worsening their status. In this patient, the PPI and PaP score indicated that he had around three weeks

left to live, suggesting that HHS treatment might increase his quality of life in his final weeks. In view of the drawbacks of large-volume fluid replacement, a relatively small volume of normal saline was administered. Subsequently, the patient showed improvements in HHS and subjective symptoms.

When a patient in palliative care complains of lethargy and nausea, cachexia is often suspected. However, symptoms suggestive of cachexia may actually denote HHS, a treatable condition. To contribute toward best supportive care for patients with end-stage diseases, physicians should conduct an appropriate test for HHS diagnosis, and proceed with treatment in a manner appropriate to the patient's condition.

Conclusion

We reported a patient under palliative care in whom HHS treatment improved the patient's symptoms. HHS should be listed as a differential diagnosis of such nonspecific symptoms as lethargy and nausea, especially in a diabetic patient with an end-stage disease.

Declaration of interest

There are no conflicts of interest to declare.

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Declaration of patient consent

The authors certify that they obtained all appropriate patient consent forms. The patient provided consent for his clinical information to be reported in the journal.

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緩和ケア目的でのコルチコステロイド投与後に認められた高浸透圧高血糖状態：症例報告

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要　約

コルチコステロイドは症状緩和のために緩和ケアで広く使用されているが，その有害事象として高血糖を示す例がある。コルチコステロイド投与中に高浸透圧高血糖状態（hyperosmolar hyperglycemic state: HHS）を発症し，嘔気・倦怠感を示した糖尿病合併末期がん患者の臨床経過を報告する。インスリン療法と補液により，患者のQOLは改善し自宅へ退院した。末期癌患者の嘔気・倦怠感の原因は悪液質に起因する例が多いが，糖尿病を有する末期癌患者がコルチコステロイド投与中に嘔気・倦怠感を示した場合，HHSを考慮すべきであることが示唆された。
（キーワード：コルチコステロイド，高浸透圧高血糖状態，糖尿病，緩和ケア）

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